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LAST RELOADED: Oct 29, 2004 (20041029/UP).

=> file caplus biosis
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FULL ESTIMATED COST                                    0.06       0.27

FILE 'CAPLUS' ENTERED AT 10:07:47 ON 31 OCT 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 10:07:47 ON 31 OCT 2004
Copyright (c) 2004 The Thomson Corporation.

=> "HIV fusion inhibitor"
L1          39 "HIV FUSION INHIBITOR"

=> CXCR4 and L1
L2           1 CXCR4 AND L1

=> "HIV fusion assay"
L3           1 "HIV FUSION ASSAY"

=> "HIV fusion"
L4         191 "HIV FUSION"

=> CXCR4 and L4
L5          20 CXCR4 AND L4

=> inhibitor and L5
L6           3 INHIBITOR AND L5

=> "beta gal"
L7        4311 "BETA GAL"

=> L7 and L4
L8           4 L7 AND L4

=> L7 and L5
L9           0 L7 AND L5

=> T-tropic"
MISMATCHED QUOTE 'T-TROPIC"'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> L1 and CXCR4
L10          1 L1 AND CXCR4

=> D L1 IBIB ABS

L1   ANSWER 1 OF 39  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2004:890602  CAPLUS
TITLE:                   HIV Fusion Inhibitor
                         Peptide T-1249 Is Able To Insert or Adsorb to Lipidic
                         Bilayers. Putative Correlation with Improved
```

Efficiency

AUTHOR(S): Veiga, A. Salome; Santos, Nuno C.; Loura, Luis M. S.; Fedorov, Aleksandre; Castanho, Miguel A. R. B.

CORPORATE SOURCE: Centro de Quimica e Bioquimica, Faculdade de Ciencias da Universidade de Lisboa, Lisbon, 1749-016, Port.

SOURCE: Journal of the American Chemical Society (2004), 126(45), 14758-14763
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB T-1249 is a **HIV fusion inhibitor** peptide under clin. trials. Its interaction with biol. membrane models (large unilamellar vesicles) was studied using fluorescence spectroscopy. A gp41 peptide that includes one of the hydrophobic terminals of T-1249 was also studied. Both peptides partition extensively to liquid-crystalline POPC (1-palmitoyl-2-oleyl-sn-glycero-3-phosphocholine) (ΔG = -7.0 kcal/mol and -8.7 kcal/mol, for T-1249 and terminal peptide, resp.) and are located at the interface of the membrane. T-1249 is essentially in a random coil conformation in this lipidic medium, although a small α-helix contribution is present. When other lipid compns. are used (DPPC, POPG + POPC, and POPC + cholesterol) (DPPC (1,2-dipalmitoyl-sn-glycero-3-phosphocholine) and POPG (1-palmitoyl-2-oleyl-sn-glycero-3-[phospho-rac-(1-glycerol)), partition decreases, the most severe effect being the presence of cholesterol. Partition expts. and fluorescence resonance energy transfer anal. show that T-1249 adsorbs to cholesterol-rich membranes. The improved clin. efficiency of T-1249 relative to enfuvirtide (T20) may be related to its bigger partition coefficient and ability to adsorb to rigid lipidic areas on the cell surface, where most receptors are inserted. Moreover, adsorption to the sterol-rich viral membrane helps to increase the local concentration of the inhibitor peptide at the fusion site.

=> D L3 IBIB abs

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:509551 CAPLUS
DOCUMENT NUMBER: 140:146468

TITLE: Minimizing the pharmacophore of a potent HIV-1 inhibitor

AUTHOR(S): Devin-Chaloin, Chantal; Moery, Lionel; Hartley, Oliver; Rose, Keith; Offord, Robin

CORPORATE SOURCE: Departement de Biochimie Medicale CMU, Geneva, Switz.

SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 389-390. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4

DOCUMENT TYPE: Conference
LANGUAGE: English

AB A symposium report. Truncated analogs of NNY-RANTES, containing a PEG-succinimide linker with good activity in **HIV fusion assay** were synthesized. The PEG-succinimide motif imitated the spatial location of the region replaced by the polyamide. These truncated analogs are useful in identifying the physico-chemical properties and the spatial location of the regions of n-nonanoyl RANTES that are responsible for its activity.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L6 IBIB ABS 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:65099 CAPLUS
TITLE: Compensatory link between fusion and endocytosis of human immunodeficiency virus type 1 in human CD4 T lymphocytes
AUTHOR(S): Schaeffer, Evelyne; Soros, Vanessa B.; Greene, Warner C.
CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, University of California, San Francisco, CA, 94141, USA
SOURCE: Journal of Virology (2004), 78(3), 1375-1383
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Virions of the type 1 human immunodeficiency virus (HIV-1) can enter target cells by fusion or endocytosis, with sharply different functional consequences. Fusion promotes productive infection of the target cell, while endocytosis generally leads to virion inactivation in acidified endosomes or degradation in lysosomes. Virion fusion and endocytosis occur equally in T cells, but these pathways have been regarded as independent because endocytosis of HIV virions requires neither CD4 nor CCR5/ **CXCR4** engagement in HeLa-CD4 cells. Using flow cytometric techniques to assess the binding and entry of green fluorescent protein (GFP)-Vpr-labeled HIV virions into primary peripheral blood mononuclear cells, we have found that **HIV fusion** and endocytosis are restricted to the CD4-expressing subset of cells and that both pathways commonly require the initial binding of HIV virions to surface CD4 receptors. Blockade of **CXCR4**-tropic HIV virion fusion with AMD3100, a **CXCR4**-specific entry **inhibitor**, increased virion entry via the endocytic pathway. Similarly, inhibition of endosome acidification with bafilomycin A1, concanamycin A, or NH4Cl enhanced entry via the fusion pathway. Although fusion remained dependent on CD4 and chemokine receptor binding, the endosome **inhibitors** did not alter surface expression of CD4 and **CXCR4**. These results suggest that fusion in the presence of the endosome **inhibitors** likely occurs within nonacidified endosomes. However, the ability of these **inhibitors** to impair vesicle trafficking from early to late endosomes in some cells could also increase the recycling of these virion-containing endosomes to the cell surface, where fusion occurs. In summary, our results reveal an unexpected, CD4-mediated reciprocal relationship between the pathways governing HIV virion fusion and endocytosis.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:353241 CAPLUS
DOCUMENT NUMBER: 135:312933
TITLE: **HIV fusion** and its inhibition
AUTHOR(S): LaBranche, C. C.; Galasso, G.; Moore, J. P.; Bolognesi, D. P.; Hirsch, M. S.; Hammer, S. M.
CORPORATE SOURCE: Department of Surgery, Duke University Medical Center, Durham, NC, USA
SOURCE: Antiviral Research (2001), 50(2), 95-115
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with many refs. covers the binding and fusion of **HIV**; **fusion inhibitors** in clin. trials; anal. of interaction between antiviral agents; guidelines for effective anti-HIV therapy; development of antiviral drugs that target HIV entry process i.e.,

inhibitors of CD4 binding, core-receptor interaction,and fusion (peptide-based fusion **inhibitors** T20 and T1249, tetramic Ig-CD4 fusion protein PRO 542 and **CXCR4** antagonist AMD3100).
REFERENCE COUNT: 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:148781 BIOSIS
DOCUMENT NUMBER: PREV200400152569
TITLE: Compensatory link between fusion and endocytosis of human immunodeficiency virus type 1 in human CD4 T lymphocytes.
AUTHOR(S): Schaeffer, Evelyne; Soros, Vanessa B.; Greene, Warner C. [Reprint Author]
CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, P.O. Box 419100, San Francisco, CA, 94141-9100, USA
wgreene@gladstone.ucsf.edu
SOURCE: Journal of Virology, (February 2004) Vol. 78, No. 3, pp. 1375-1383. print.
ISSN: 0022-538X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004
AB Virions of the type 1 human immunodeficiency virus (HIV-1) can enter target cells by fusion or endocytosis, with sharply different functional consequences. Fusion promotes productive infection of the target cell, while endocytosis generally leads to virion inactivation in acidified endosomes or degradation in lysosomes. Virion fusion and endocytosis occur equally in T cells, but these pathways have been regarded as independent because endocytosis of HIV virions requires neither CD4 nor CCR5/**CXCR4** engagement in HeLa-CD4 cells. Using flow cytometric techniques to assess the binding and entry of green fluorescent protein (GFP)-Vpr-labeled HIV virions into primary peripheral blood mononuclear cells, we have found that **HIV fusion** and endocytosis are restricted to the CD4-expressing subset of cells and that both pathways commonly require the initial binding of HIV virions to surface CD4 receptors. Blockade of **CXCR4**-tropic HIV virion fusion with AMD3100, a **CXCR4**-specific entry **inhibitor**, increased virion entry via the endocytic pathway. Similarly, inhibition of endosome acidification with bafilomycin A1, concanamycin A, or NH4Cl enhanced entry via the fusion pathway. Although fusion remained dependent on CD4 and chemokine receptor binding, the endosome **inhibitors** did not alter surface expression of CD4 and **CXCR4**. These results suggest that fusion in the presence of the endosome **inhibitors** likely occurs within nonacidified endosomes. However, the ability of these **inhibitors** to impair vesicle trafficking from early to late endosomes in some cells could also increase the recycling of these virion-containing endosomes to the cell surface, where fusion occurs. In summary, our results reveal an unexpected, CD4-mediated reciprocal relationship between the pathways governing HIV virion fusion and endocytosis.

=> D L8 IBIB ABS 1-4

L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:7020 CAPLUS
DOCUMENT NUMBER: 126:46359
TITLE: Tryptophan regulated expression and aqueous two-phase separation of recombinant **HIV-fusion** peptides
AUTHOR(S): Pulliam, Tracey R.; Winston, Scott; Bentley, William E.

CORPORATE SOURCE: Center Agricultural Biotechnology, Univ. Maryland, College Park, MD, 20742, USA
SOURCE: Enzyme and Microbial Technology (1997), 20(1), 46-51
CODEN: EMTED2; ISSN: 0141-0229
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study investigates the expression and separation of a recombinant HIV-. **beta.-gal** fusion protein expressed in Escherichia coli under trp promoter control. Product expression and its sensitivity to proteolytic degradation are correlated with inducer strength and protease activity. Two previously unreported proteolytic activities of 42 and 55 kDa mol. weight were revealed which were shown to have activity towards . **beta.-gal**. Furthermore, by taking advantage of the extreme partitioning behavior of β-galactosidase the HIV-. **beta.-gal** fusion was separated and partially purified in a polyethylene glycol-potassium phosphate aqueous two-phase system. Addnl., the 55 kDa protease with .**beta.-gal** specificity partitioned into the salt-rich bottom phase.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:19715 CAPLUS
DOCUMENT NUMBER: 124:105735
TITLE: Characterization of siamycin I, a human immunodeficiency virus fusion inhibitor
AUTHOR(S): Lin, Ping-Fang; Samanta, Himadri; Bechtold, Clifford M.; Deminie, Carol A.; Patick, Amy K.; Alam, Masud; Riccardi, Keith; Rose, Ronald E.; White, Richard J.; Colonno, Richard J.
CORPORATE SOURCE: Dep. Virol., Bristol-Myers Squibb Pharmaceutical Res. Inst., Wallingford, CT, 06492, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1996), 40(1), 133-8
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The human immunodeficiency virus (**HIV**) **fusion** inhibitor siamycin I, a 21-residue tricyclic peptide, was identified from a Streptomyces culture by using a cell fusion assay involving cocultivation of HeLa-CD4+ cells and monkey kidney (BSC-1) cells expressing the HIV envelope gp160. Siamycin I is effective against acute HIV type 1 (HIV-1) and HIV-2 infections, with 50% EDs ranging from 0.05 to 5.7 μM, and the concentration resulting in a 50% decrease in cell viability in the absence of viral infection is 150 μM in CEM-SS cells. Siamycin I inhibits fusion between C8166 cells and CEM-SS cells chronically infected with HIV (50% ED of 0.08 μM) but has no effect on Sendai virus-induced fusion or murine myoblast fusion. Siamycin I does not inhibit gp120 binding to CD4 in either gp120- or CD4-based capture enzyme-linked immunosorbent assays. Inhibition of HIV-induced fusion by this compound is reversible, suggesting that siamycin I binds noncovalently. An HIV-1 resistant variant was selected by in vitro passage of virus in the presence of increasing concns. of siamycin I. Drug susceptibility studies on a chimeric virus containing the envelope gene from the siamycin I-resistant variant indicate that resistance maps to the gp160 gene. Envelope-deficient HIV complemented with gp160 from siamycin I-resistant HIV also displayed a resistant phenotype upon infection of HeLa-CD4-LTR-. **beta.-gal** cells. A comparison of the DNA sequences of the envelope genes from the resistant and parent viruses revealed a total of six amino acid changes. Together these results indicate that siamycin I interacts with the HIV envelope protein.

L8 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1997:64185 BIOSIS
DOCUMENT NUMBER: PREV199799363388
TITLE: Tryptophan regulated expression and aqueous two-phase separation of recombinant **HIV-fusion** peptides.
AUTHOR(S): Pulliam, Tracey R.; Winston, Scott; Bentley, William E. [Reprint author]
CORPORATE SOURCE: Dep. Chemical Engineering, Univ. Maryland, Cent. Agric. Biotechnol., College Park, MD 20742, USA
SOURCE: Enzyme and Microbial Technology, (1997) Vol. 20, No. 1, pp. 46-51.
CODEN: EMTED2. ISSN: 0141-0229.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 1997
Last Updated on STN: 11 Feb 1997

AB This study investigates the expression and separation of a recombinant HIV-**beta-gal** fusion protein expressed in Escherichia coli wider trp promoter controL Product expression and its sensitivity to proteolytic degradation are correlated with inducer strength and protease activity. Two previously unreported proteolytic activities of 42 and 55 kDa molecular weight were revealed which were shown to have activity towards **beta-gal**. Furthermore, by taking advantage of the extreme partitioning behavior of beta-galactosidase, the HIV-**beta-gal** fusion was separated and partially purified in a polyethylene glycol-potassium phosphate aqueous two-phase system. Additionally, the 55 kDa protease with **beta-gal** specificity partitioned into the salt-rich bottom phase.

L8 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1996:73061 BIOSIS
DOCUMENT NUMBER: PREV199698645196
TITLE: Characterization of siamycin I, a human immunodeficiency virus fusion inhibitor.
AUTHOR(S): Lin, Pin-Fang [Reprint author]; Samanta, Himadri; Bechtold, Clifford M.; Deminie, Carol A.; Patick, Amy K.; Alam, Masud; Riccardi, Keith; Rose, Ronald E.; White, Richard J.; Colonno, Richard J.
CORPORATE SOURCE: Bristol-Myeres Squibb Co., 5 Research Parkway, Wallingford, CT 06492, USA
SOURCE: Antimicrobial Agents and Chemotherapy, (1996) Vol. 40, No. 1, pp. 133-138.
CODEN: AMACCQ. ISSN: 0066-4804.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Feb 1996
Last Updated on STN: 27 Feb 1996

AB The human immunodeficiency virus (**HIV**) **fusion** inhibitor siamycin I, a 21-residue tricyclic peptide, was identified from a Streptomyces culture by using a cell fusion assay involving cocultivation of HeLa-CD4+ cells and monkey kidney (BSC-1) cells expressing the HIV envelope gp160. Siamycin I is effective against acute HIV type 1 (HIV-1) and HIV-2 infections, with 50% effective doses ranging from 0.05 to 5.7 mu-M, and the concentration resulting in a 50% decrease in cell viability in the absence of viral infection is 150 mu-M in CEM-SS cells. Siamycin I inhibits fusion between C8166 cells and CEM-SS cells chronically infected with HIV (50% effective dose of 0.08 mu-M) but has no effect on Sendai virus-induced fusion or murine myoblast fusion. Siamycin I does not inhibit gp120 binding to CD4 in either gp120- or CD4-based capture enzyme-linked immunosorbent assays. Inhibition of HIV-induced fusion by this compound is reversible, suggesting that siamycin I binds noncovalently. An HIV-1 resistant variant was selected by in vitro passage of virus in the presence of increasing concentrations of siamycin

I. Drug susceptibility studies on a chimeric virus containing the envelope gene from the siamycin I-resistant variant indicate that resistance maps to the gp160 gene. Envelope-deficient HIV complemented with gp160 from siamycin I-resistant HIV also displayed a resistant phenotype upon infection of HeLa-CD4-LTR-**beta-gal** cells. A comparison of the DNA sequences of the envelope genes from the resistant and parent viruses revealed a total of six amino acid changes. Together these results indicate that siamycin I interacts with the HIV envelope protein.

=> D L5 IBIB 1-20

L5 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:698214 CAPLUS
DOCUMENT NUMBER: 141:218921
TITLE: HIV-specific fusion proteins comprising cellular gp120-binding co-receptor and receptor proteins and a viral receptor protein and therapeutic and diagnostic uses
INVENTOR(S): Glass, David J.; Karow, Margaret; Smith, Eric
PATENT ASSIGNEE(S): Regeneron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072233	A2	20040826	WO 2004-US2650	20040130
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004214285	A1	20041028	US 2004-768932	20040130
PRIORITY APPLN. INFO.:			US 2003-446347P	P 20030210

L5 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:65099 CAPLUS
TITLE: Compensatory link between fusion and endocytosis of human immunodeficiency virus type 1 in human CD4 T lymphocytes
AUTHOR(S): Schaeffer, Evelyne; Soros, Vanessa B.; Greene, Warner C.
CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, University of California, San Francisco, CA, 94141, USA
SOURCE: Journal of Virology (2004), 78(3), 1375-1383
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:900264 CAPLUS
DOCUMENT NUMBER: 140:92158
TITLE: Establishment of an HIV cell-cell fusion assay by using two genetically modified HeLa cell lines and reporter gene
AUTHOR(S): Sakamoto, Tatsunori; Ushijima, Hiroshi; Okitsu, Shoko; Suzuki, Eiko; Sakai, Koji; Morikawa, Shigeru; Muller, Werner E. G.
CORPORATE SOURCE: Graduate School of Medicine, Department of Developmental Medical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Journal of Virological Methods (2003), 114(2), 159-166
CODEN: JVMEDH; ISSN: 0166-0934
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:637536 CAPLUS
DOCUMENT NUMBER: 137:179855
TITLE: Methods and compositions using gp120 peptides for inhibiting HIV-coreceptor interactions
INVENTOR(S): Chertov, Oleg; Oppenheim, Joost J.; Chen, Xin; Mcgrath, Connor; Sowder, Raymond C., II; Lubkowski, Jacek; Wetzel, Michele; Rogers, Thomas J.
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Secretary of the Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064154	A2	20020822	WO 2002-US5063	20020215
WO 2002064154	A3	20030424		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1361886	A2	20031119	EP 2002-723190	20020215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-269534P P 20010215
WO 2002-US5063 W 20020215

L5 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:783672 CAPLUS
DOCUMENT NUMBER: 136:68562
TITLE: Antigenic properties of the human immunodeficiency virus envelope during cell-cell fusion

AUTHOR(S): Finnegan, Catherine M.; Berg, Werner; Lewis, George K.; DeVico, Anthony L.
CORPORATE SOURCE: Institute of Human Virology, University of Maryland Biotechnology Institute, Baltimore, MD, 21201, USA
SOURCE: Journal of Virology (2001), 75(22), 11096-11105
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:546466 CAPLUS
DOCUMENT NUMBER: 135:255994
TITLE: Optimal inhibition of X4 HIV isolates by the CXC chemokine stromal cell-derived factor 1α requires interaction with cell surface heparan sulfate proteoglycans
AUTHOR(S): Valenzuela-Fernandez, Agustin; Palanche, Tania; Amara, Ali; Magerus, Aude; Altmeyer, Ralf; Delaunay, Thierry; Virelizier, Jean-Louis; Baleux, Francoise; Galzi, Jean-Luc; Arenzana-Seisdedos, Fernando
CORPORATE SOURCE: Unite d'Immunologie Virale, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Journal of Biological Chemistry (2001), 276(28), 26550-26558
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:353241 CAPLUS
DOCUMENT NUMBER: 135:312933
TITLE: **HIV fusion** and its inhibition
AUTHOR(S): LaBranche, C. C.; Galasso, G.; Moore, J. P.; Bolognesi, D. P.; Hirsch, M. S.; Hammer, S. M.
CORPORATE SOURCE: Department of Surgery, Duke University Medical Center, Durham, NC, USA
SOURCE: Antiviral Research (2001), 50(2), 95-115
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:76593 CAPLUS
DOCUMENT NUMBER: 134:251061
TITLE: Role of glycosphingolipid microdomains in CD4-dependent HIV-1 fusion
AUTHOR(S): Fantini, Jacques; Hammache, Djilali; Pieroni, Gerard; Yahi, Nouara
CORPORATE SOURCE: Laboratoire de Biochimie et Biologie de la Nutrition, ESA-CNRS 6033, Faculte des Sciences de St Jerome, Marseille, 13397, Fr.
SOURCE: Glycoconjugate Journal (2001), Volume Date 2000, 17(3/4), 199-204

CODEN: GLJOEW; ISSN: 0282-0080
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:287383 CAPLUS
DOCUMENT NUMBER: 133:295264
TITLE: Interleukin-2 up-regulates expression of the human immunodeficiency virus fusion coreceptor CCR5 by CD4+ lymphocytes in vivo
AUTHOR(S): Weissman, Drew; Dybul, Mark; Daucher, Mary Beth; Davey, Richard T., Jr.; Walker, Robert E.; Kovacs, Joseph A.
CORPORATE SOURCE: Division of Infectious Diseases, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Journal of Infectious Diseases (2000), 181(3), 933-938
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:30063 CAPLUS
DOCUMENT NUMBER: 132:345932
TITLE: New reporter cell lines to study macrophage-tropic HIV envelope protein-mediated cell-cell fusion
AUTHOR(S): Hong, Yu-Long; Wu, Lan-Hsin; Cui, Mei; McMaster, Gary; Hunt, Stephen W., III; Chung, Fu-Zon
CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of the Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SOURCE: AIDS Research and Human Retroviruses (1999), 15(18), 1667-1672
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:765628 CAPLUS
DOCUMENT NUMBER: 130:138168
TITLE: The neutral glycosphingolipid globotriaosylceramide promotes fusion mediated by a CD4-dependent **CXCR4**-utilizing HIV type 1 envelope glycoprotein
AUTHOR(S): Puri, Anu; Hug, Peter; Jernigan, Kristine; Barchi, Joseph; Kim, Hee-Yong; Hamilton, Jillon; Wiels, Joelle; Murray, Gary J.; Brady, Roscoe O.; Blumenthal, Robert
CORPORATE SOURCE: Section of Membrane Structure and Function, Laboratory of Experimental and Computational Biology, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, Frederick, MD, 21702, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(24), 14435-14440
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal

LANGUAGE: English
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:129239 CAPLUS
DOCUMENT NUMBER: 128:269372
TITLE: Recombinant human CXC-chemokine receptor-4 in melanophores are linked to Gi protein: seven transmembrane coreceptors for human immunodeficiency virus entry into cells
AUTHOR(S): Chen, Wen-Ji; Jayawickreme, Channa; Watson, Chris; Wolfe, Larry; Holmes, William; Ferris, Robert; Armour, Susan; Dallas, Walter; Chen, Grace; Boone, Larry; Luther, Michael; Kenakin, Terry
CORPORATE SOURCE: Department of Molecular Sciences, Glaxo Wellcome Research and Development, Research Triangle Park, NC, 27709, USA
SOURCE: Molecular Pharmacology (1998), 53(2), 177-181
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:395183 CAPLUS
DOCUMENT NUMBER: 127:120601
TITLE: Evolution of HIV-1 coreceptor usage through interactions with distinct CCR5 and **CXCR4** domains
AUTHOR(S): Lu, Zhao-hai; Berson, Joanne F.; Chen, Ying-hua; Turner, Julie D.; Zhang, Tian-yuan; Sharron, Matthew; Jenks, M. Harley; Wang, Zi-xuan; Kim, Jin; Rucker, Joseph; Hoxie, James A.; Peiper, Stephen C.; Doms, Robert W.
CORPORATE SOURCE: James Graham Brown Cancer Center, University Louisville, Louisville, KY, 40202, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(12), 6426-6431
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:251532 CAPLUS
DOCUMENT NUMBER: 126:316221
TITLE: Differential regulation of HIV-1 fusion cofactor expression by CD28 costimulation of CD4+ T cells
AUTHOR(S): Carroll, Richard G.; Riley, James L.; Levine, Bruce L.; Feng, Yu; Kaushal, Sumesh; Ritchey, David W.; Bernstein, Wendy; Weislow, Owen S.; Brown, Charles R.; Berger, Edward A.; June, Carl H.; St. Louis, Daniel C.
CORPORATE SOURCE: Henry M. Jackson Foundation Advancement Military Med., Rockville, MD, 20850, USA
SOURCE: Science (Washington, D. C.) (1997), 276(5310), 273-276
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:250299 CAPLUS
DOCUMENT NUMBER: 126:316023
TITLE: **HIV fusion** cofactors. The chemokine receptor connection
AUTHOR(S): Uchida, Hiroyuki; Berger, Edward A.
CORPORATE SOURCE: Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: Jikken Igaku (1997), 15(2), 125-130
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

L5 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:57315 CAPLUS
DOCUMENT NUMBER: 126:88231
TITLE: Inhibition of human immunodeficiency virus fusion by a monoclonal antibody to a coreceptor (**CXCR4**) is both cell type and virus strain dependent
AUTHOR(S): McKnight, Aine; Wilkinson, David; Simmons, Graham; Talbot, Simon; Picard, Laurent; Ahuja, Mena; Marsh, Mark; Hoxie, James A.; Clapham, Paul R.
CORPORATE SOURCE: Chester Beatty Laboratories, Institute of Cancer Research, London, SW3 6JB, UK
SOURCE: Journal of Virology (1997), 71(2), 1692-1696
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:148781 BIOSIS
DOCUMENT NUMBER: PREV200400152569
TITLE: Compensatory link between fusion and endocytosis of human immunodeficiency virus type 1 in human CD4 T lymphocytes.
AUTHOR(S): Schaeffer, Evelyne; Soros, Vanessa B.; Greene, Warner C. [Reprint Author]
CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, P.O. Box 419100, San Francisco, CA, 94141-9100, USA
wgreene@gladstone.ucsf.edu
SOURCE: Journal of Virology, (February 2004) Vol. 78, No. 3, pp. 1375-1383. print.
ISSN: 0022-538X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

L5 ANSWER 18 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:76039 BIOSIS
DOCUMENT NUMBER: PREV200400077333
TITLE: Establishment of an HIV cell-cell fusion assay by using two genetically modified HeLa cell lines and reporter gene.
AUTHOR(S): Sakamoto, Tatsunori; Ushijima, Hiroshi [Reprint Author]; Okitsu, Shoko; Suzuki, Eiko; Sakai, Koji; Morikawa, Shigeru; Muller, Werner E. G.

CORPORATE SOURCE: Department of Developmental Medical Sciences, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan
ushijima@m.u-tokyo.ac.jp
SOURCE: Journal of Virological Methods, (December 2003) Vol. 114, No. 2, pp. 159-166. print.
CODEN: JVMEDH. ISSN: 0166-0934.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004

L5 ANSWER 19 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:528897 BIOSIS
DOCUMENT NUMBER: PREV200100528897
TITLE: Antigenic properties of the human immunodeficiency virus envelope during cell-cell fusion.
AUTHOR(S): Finnegan, Catherine M.; Berg, Werner; Lewis, George K.; DeVico, Anthony L. [Reprint author]
CORPORATE SOURCE: Institute of Human Virology, 725 W. Lombard St., N649, Baltimore, MD, 21201, USA
devico@umbi.umd.edu
SOURCE: Journal of Virology, (November, 2001) Vol. 75, No. 22, pp. 11096-11105. print.
CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Nov 2001
Last Updated on STN: 23 Feb 2002

L5 ANSWER 20 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:77292 BIOSIS
DOCUMENT NUMBER: PREV200000077292
TITLE: New reporter cell lines to study macrophage-tropic HIV envelope protein-mediated cell-cell fusion.
AUTHOR(S): Hong, Yu-Long; Wu, Lan-Hsin; Cui, Mei; McMaster, Gary; Hunt, Stephen W., III; Chung, Fu-Zon [Reprint author]
CORPORATE SOURCE: Department of Molecular Biology, Parke-Davis Pharmaceutical Research, 2800 Plymouth Rd., Ann Arbor, MI, USA
SOURCE: AIDS Research and Human Retroviruses, (Dec., 1999) Vol. 15, No. 18, pp. 1667-1672. print.
CODEN: ARHRE7. ISSN: 0889-2229.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Feb 2000
Last Updated on STN: 3 Jan 2002

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L5 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:698214 CAPLUS
DOCUMENT NUMBER: 141:218921
TITLE: HIV-specific fusion proteins comprising cellular gp120-binding co-receptor and receptor proteins and a viral receptor protein and therapeutic and diagnostic uses
INVENTOR(S): Glass, David J.; Karow, Margaret; Smith, Eric
PATENT ASSIGNEE(S): Regeneron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072233	A2	20040826	WO 2004-US2650	20040130

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004214285	A1	20041028	US 2004-768932	20040130

PRIORITY APPLN. INFO.: US 2003-446347P P 20030210

AB The present invention provides a HIV-specific fusion protein (also termed an "HIV trap") capable of binding the Human Immunodeficiency Virus (HIV), which prevents or inhibits the virus from cell entry. The HIV-specific fusion protein comprises: (a) one or more domains of a cellular gp120-binding co-receptor protein; (b) one or more domains of a cellular gp120-binding receptor protein; and optionally (c) a multimerizing component; and (d) one or more domains of a viral protein. As a functional equivalent of (a) or (b) an Ig-VH immunospecific for gp120 could be used. In specific embodiments, the co-receptor protein is human CCR5, **CXCR4**, or DC-SIGN, or gp120-binding domain thereof, and receptor protein is human CD4, or its Ig-like domain. The viral protein is a viral receptor, and more specifically fragment of the second helical region of receptor gp41. In specific embodiments, the HIV-specific fusion protein is a multimer capable of binding an HIV particle, and is useful for the treatment of HIV infections. The HIV-specific fusion proteins of the invention are further useful for detecting HIV in a variety of in vitro and in vivo diagnostic and prognostic assays.

L5 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:65099 CAPLUS
TITLE: Compensatory link between fusion and endocytosis of human immunodeficiency virus type 1 in human CD4 T lymphocytes
AUTHOR(S): Schaeffer, Evelyne; Soros, Vanessa B.; Greene, Warner C.
CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, University of California, San Francisco, CA, 94141, USA
SOURCE: Journal of Virology (2004), 78(3), 1375-1383
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Virions of the type 1 human immunodeficiency virus (HIV-1) can enter target cells by fusion or endocytosis, with sharply different functional consequences. Fusion promotes productive infection of the target cell, while endocytosis generally leads to virion inactivation in acidified endosomes or degradation in lysosomes. Virion fusion and endocytosis occur equally in T cells, but these pathways have been regarded as independent because endocytosis of HIV virions requires neither CD4 nor CCR5/ **CXCR4** engagement in HeLa-CD4 cells. Using flow cytometric techniques to assess the binding and entry of green fluorescent protein (GFP)-Vpr-labeled HIV virions into primary peripheral blood mononuclear

cells, we have found that **HIV fusion** and endocytosis are restricted to the CD4-expressing subset of cells and that both pathways commonly require the initial binding of HIV virions to surface CD4 receptors. Blockade of **CXCR4**-tropic HIV virion fusion with AMD3100, a **CXCR4**-specific entry inhibitor, increased virion entry via the endocytic pathway. Similarly, inhibition of endosome acidification with bafilomycin A1, concanamycin A, or NH4Cl enhanced entry via the fusion pathway. Although fusion remained dependent on CD4 and chemokine receptor binding, the endosome inhibitors did not alter surface expression of CD4 and **CXCR4**. These results suggest that fusion in the presence of the endosome inhibitors likely occurs within nonacidified endosomes. However, the ability of these inhibitors to impair vesicle trafficking from early to late endosomes in some cells could also increase the recycling of these virion-containing endosomes to the cell surface, where fusion occurs. In summary, our results reveal an unexpected, CD4-mediated reciprocal relationship between the pathways governing HIV virion fusion and endocytosis.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:900264 CAPLUS

DOCUMENT NUMBER: 140:92158

TITLE: Establishment of an HIV cell-cell fusion assay by using two genetically modified HeLa cell lines and reporter gene

AUTHOR(S): Sakamoto, Tatsunori; Ushijima, Hiroshi; Okitsu, Shoko; Suzuki, Eiko; Sakai, Koji; Morikawa, Shigeru; Muller, Werner E. G.

CORPORATE SOURCE: Graduate School of Medicine, Department of Developmental Medical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan

SOURCE: Journal of Virological Methods (2003), 114(2), 159-166
CODEN: JVMEDH; ISSN: 0166-0934

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Infection of human cells with the human immunodeficiency virus type I (HIV-1) can be mimicked by a fusion process between cells expressing the HIV envelope protein (Env) and cells expressing both human CD4 together with the appropriate human chemokine receptors. In this study, a T-tropic HIV cell-cell fusion assay was established that utilized CD4, human **CXCR4** and HIV NL4-3 gp160 as fusion components and a T7 polymerase-activated luciferase as a reporter system. The HeLa T4 cells used, expressed CD4 and **CXCR4**, and the applied HeLa KS386 cells expressed HIV NL4-3 gp160. By combining HeLa T4 cells with HeLa KS386 cells, an approx. about 100- to 300-fold increase in luciferase activity could be elicited relative to the control. The addition of anti-CD4 monoclonal antibody (Mab) (RPA-T4) or anti-**CXCR4** Mab (12G5) in the assay significantly inhibited the fusion event; in contrast, an anti-CCR5 Mab (2D7) had no effect, indicating that the fusion assay was CD4 and **CXCR4** dependent. In this report, fusion events could be monitored by both the luciferase reporter system and syncytia formation. Fusion events were monitored and compared using these two approaches. The luciferase reporter system was found to be more sensitive than syncytia formation. Moreover, compared with previous **HIV fusion** models, such as using recombinant vaccinia viruses, this system has several advantages, including simplicity and sensitivity. Finally, the system provides a powerful tool to study fusion mechanisms mediated by T-tropic HIV gp160, as well as to screen for fusion-blocking antibodies and antiviral agents.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:637536 CAPLUS
DOCUMENT NUMBER: 137:179855
TITLE: Methods and compositions using gp120 peptides for inhibiting HIV-coreceptor interactions
INVENTOR(S): Chertov, Oleg; Oppenheim, Joost J.; Chen, Xin; Mcgrath, Connor; Sowder, Raymond C., II; Lubkowski, Jacek; Wetzel, Michele; Rogers, Thomas J.
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Secretary of the Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064154	A2	20020822	WO 2002-US5063	20020215
WO 2002064154	A3	20030424		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1361886	A2	20031119	EP 2002-723190	20020215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-269534P P 20010215
WO 2002-US5063 W 20020215

AB Methods and compns. are provided for inhibiting interactions between human immunodeficiency viruses (HIVs) and viral coreceptors, including **CXCR4** and/or CCR5 coreceptors. The anti-coreceptor binding agent includes a peptide portion of the gp120 envelope protein of HIV-1, as well as peptide analogs and mimetics of this peptide, that specifically binds to, or modulates activity of, the coreceptors(s). The anti-coreceptor binding agent is useful as a prophylactic or therapeutic treatment to prevent or inhibit HIV binding to a susceptible cell and thereby reduces infection and/or moderates or treats related diseases. In alternative embodiments, the peptides, analogs and mimetics are effective to inhibit direct co-receptor binding by HIV virus, coreceptor binding by HIV gp 120 proteins or peptides, **HIV fusion** with target host cells, HIV virion entry into host cells, HIV replication, and HIV transmission between cells and hosts. In more detailed embodiments, the anti-coreceptor binding agents of the invention are multi-tropic by exhibiting activity against HIV interactions with multiple, **CXCR4** and CCR5, coreceptors.

L5 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:783672 CAPLUS
DOCUMENT NUMBER: 136:68562
TITLE: Antigenic properties of the human immunodeficiency virus envelope during cell-cell fusion
AUTHOR(S): Finnegan, Catherine M.; Berg, Werner; Lewis, George K.; DeVico, Anthony L.
CORPORATE SOURCE: Institute of Human Virology, University of Maryland Biotechnology Institute, Baltimore, MD, 21201, USA

SOURCE: Journal of Virology (2001), 75(22), 11096-11105
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human immunodeficiency virus (**HIV**) **fusion** and entry involves sequential interactions between the viral envelope protein, gp120, cell surface CD4, and a G-protein-coupled coreceptor. Each interaction creates an intermediate gp120 structure predicted to display distinct antigenic features, including key functional domains for viral entry. In this study, we examined the disposition of these features during the fusion of HeLa cells expressing either HIVHXB2 envelope (Env cells) or **CXCR4** and CD4 (target cells). Cell-cell fusion, indicated by cytoplasmic dye transfer, was allowed to progress for various times and then arrested. The cells were then examined for reactivity with antibodies directed against receptor-induced epitopes on gp120. Analyses of cells arrested by cooling to 4°C revealed that antibodies against the CD4-induced coreceptor-binding domain, i.e., 17b, 48d, and CG10, faintly react with Env cells even in the absence of target cell or soluble CD4 (sCD4) interactions. Such reactivity increased after exposure to sCD4 but remained unchanged during fusion with target cells and was not intensified at the Env-target cell interface. Notably, the antibodies did not react with Env cells when treated with a covalent cross-linker either alone or during fusion with target cells. Immunoreactivity could not be promoted or otherwise altered on either temperature arrested or cross-linked cells by preventing coreceptor interactions or by using a 17b Fab. In comparison, two other gp120-CD4 complex-dependent antibodies against epitopes outside the coreceptor domain, 8F101 and A32, exhibited a different pattern of reactivity. These antibodies reacted with the Env-target cell interface only after 30 min of cocultivation, concurrent with the first visible transfer of cytoplasmic dye from Env to target cells. At later times, the staining surrounded entire syncytia. Such binding was entirely dependent on the formation of gp120-CD4-**CXCR4** tricomplexes since staining was absent with SDF-treated or coreceptor-neg. target cells. Overall, these studies show that access to the CD4-induced coreceptor-binding domain on gp120 is largely blocked at the fusing cell interface and is unlikely to represent a target for neutralizing antibodies. However, new epitopes are presented on intermediate gp120 structures formed as a result of coreceptor interactions. Such findings have important implications for HIV vaccine approaches based on conformational alterations in envelope structures.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:546466 CAPLUS
DOCUMENT NUMBER: 135:255994
TITLE: Optimal inhibition of X4 HIV isolates by the CXC chemokine stromal cell-derived factor 1α requires interaction with cell surface heparan sulfate proteoglycans
AUTHOR(S): Valenzuela-Fernandez, Agustin; Palanche, Tania; Amara, Ali; Magerus, Aude; Altmeyer, Ralf; Delaunay, Thierry; Virelizier, Jean-Louis; Baleux, Francoise; Galzi, Jean-Luc; Arenzana-Seisdedos, Fernando
CORPORATE SOURCE: Unite d'Immunologie Virale, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Journal of Biological Chemistry (2001), 276(28), 26550-26558
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chemokine stromal cell-derived factor 1 (SDF-1) is the natural ligand for CXC chemokine receptor 4 (**CXCR4**). SDF-1 inhibits infection of CD4+ cells by X4 (**CXCR4**-dependent) human immunodeficiency virus (HIV) strains. We previously showed that SDF-1α interacts specifically with heparin or heparan sulfates (HSs). Herein, we delimited the boundaries of the HS-binding domain located in the first β-strand of SDF-1α as the critical residues. We also provide evidence that binding to cell surface heparan sulfate proteoglycans (HSPGs) dets. the capacity of SDF-1α to prevent the fusogenic activity of HIV-1 X4 isolates in leukocytes. Indeed, SDF-1α mutants lacking the capacity to interact with HSPGs showed a substantially reduced capacity to prevent cell-to-cell fusion mediated by X4 HIV envelope glycoproteins. Moreover, the enzymic removal of cell surface HS diminishes the HIV-inhibitory capacity of the chemokine to the levels shown by the HS-binding-disabled mutant counterparts. The mechanisms underlying the optimal HIV-inhibitory activity of SDF-1α when attached to HSPGs were investigated. Combining fluorescence resonance energy transfer and laser confocal microscopy, we demonstrate the concomitant binding of SDF-1α to **CXCR4** and HSPGs at the cell membrane. Using FRET between a Texas Red-labeled SDF-1α and an enhanced green fluorescent protein-tagged **CXCR4**, we show that binding of SDF-1α to cell surface HSPGs modifies neither the kinetics of occupancy nor activation in real time of **CXCR4** by the chemokine. Moreover, attachment to HSPGs does not modify the potency of the chemokine to promote internalization of **CXCR4**. Attachment to cellular HSPGs may cooperate in the optimal anti-HIV activity of SDF-1α by increasing the local concentration of the chemokine in the surrounding environment of **CXCR4**, thus facilitating sustained occupancy and down-regulation of the HIV coreceptor.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:353241 CAPLUS
DOCUMENT NUMBER: 135:312933
TITLE: **HIV fusion** and its inhibition
AUTHOR(S): LaBranche, C. C.; Galasso, G.; Moore, J. P.; Bolognesi, D. P.; Hirsch, M. S.; Hammer, S. M.
CORPORATE SOURCE: Department of Surgery, Duke University Medical Center, Durham, NC, USA
SOURCE: Antiviral Research (2001), 50(2), 95-115
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with many refs. covers the binding and fusion of **HIV**; **fusion** inhibitors in clin. trials; anal. of interaction between antiviral agents; guidelines for effective anti-HIV therapy; development of antiviral drugs that target HIV entry process i.e., inhibitors of CD4 binding, core-receptor interaction,and fusion (peptide-based fusion inhibitors T20 and T1249, tetramic Ig-CD4 fusion protein PRO 542 and **CXCR4** antagonist AMD3100).

REFERENCE COUNT: 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:76593 CAPLUS
DOCUMENT NUMBER: 134:251061
TITLE: Role of glycosphingolipid microdomains in CD4-dependent HIV-1 fusion
AUTHOR(S): Fantini, Jacques; Hammache, Djilali; Pieroni, Gerard; Yahi, Nouara
CORPORATE SOURCE: Laboratoire de Biochimie et Biologie de la Nutrition,

ESA-CNRS 6033, Faculte des Sciences de St Jerome, Marseille, 13397, Fr.

SOURCE: Glycoconjugate Journal (2001), Volume Date 2000, 17(3/4), 199-204
CODEN: GLJOEW; ISSN: 0282-0080

PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The fusion of HIV-1 with the plasma membrane of CD4+ cells is triggered by the interaction of HIV-1 surface envelope glycoprotein gp120 with the CD4 receptor, and requires coreceptors (CCR5 and **CXCR4**). Recent advances in the study of HIV-1 entry into CD4+ cells suggest that glycosphingolipids (GSL) may also participate in the fusion process. GSL are organized in functional microdomains which are associated with specific membrane proteins such as CD4. GSL-enriched microdomains were purified from human lymphocytes and reconstituted as a monomol. film at the air-water interface of a Langmuir film balance. Surface pressure measurements allowed to characterize the sequential interaction of GSL with CD4 and with gp120. Using this approach, the authors identified globotriaosylceramide (Gb3) and ganglioside GM3 as the main lymphocyte GSL recognized by gp120. In both cases, the interaction was saturable and dramatically increased by CD4. The authors propose that GSL microdomains behave as moving platforms allowing the recruitment of HIV-1 coreceptors after the initial interaction between the viral particle and CD4. According to this model, the GSL microdomain may: (1) stabilize the attachment of the virus with the cell surface via multiple low affinity interactions between the V3 domain of gp120 and the carbohydrate moiety of GSL, and (2) convey the virus to an appropriate coreceptor by moving freely in the outer leaflet of the plasma membrane. This model can be extrapolated to all envelope viruses (e.g. influenza virus) that use cell surface GSL of the host cells as receptors or coreceptors.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:287383 CAPLUS
DOCUMENT NUMBER: 133:295264
TITLE: Interleukin-2 up-regulates expression of the human immunodeficiency virus fusion coreceptor CCR5 by CD4+ lymphocytes in vivo
AUTHOR(S): Weissman, Drew; Dybul, Mark; Daucher, Mary Beth; Davey, Richard T., Jr.; Walker, Robert E.; Kovacs, Joseph A.
CORPORATE SOURCE: Division of Infectious Diseases, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Journal of Infectious Diseases (2000), 181(3), 933-938
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intermittent interleukin-2 (IL-2) therapy can substantially increase CD4+ T cell counts of human immunodeficiency virus (HIV)-infected subjects. Administration of IL-2 led to transient up-regulation of CCR5 on CD4+ T cells; up to 87% of CD4+ cells expressed CCR5 after a 5-day cycle, with return to baseline levels within 2 wk. Unlike in vitro studies, CCR5 was coexpressed with CD45RA and **CXCR4** on CD4+ T cells after IL-2 therapy. The observed increase in coreceptor expression was not associated with detectable increases in viral replication. IL-2 therapy induced CCR5 expression in >90% of circulating memory CD4+ T cells, determined to be a long-term reservoir of HIV, suggesting significant activation of these cells. These studies demonstrate that levels of expression of HIV coreceptors alone do not always correlate with HIV replication in vivo and that IL-2 therapy activates a majority of memory T cells in the

circulation and likely throughout the immune system.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:30063 CAPLUS
DOCUMENT NUMBER: 132:345932
TITLE: New reporter cell lines to study macrophage-tropic HIV envelope protein-mediated cell-cell fusion
AUTHOR(S): Hong, Yu-Long; Wu, Lan-Hsin; Cui, Mei; McMaster, Gary; Hunt, Stephen W., III; Chung, Fu-Zon
CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of the Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SOURCE: AIDS Research and Human Retroviruses (1999), 15(18), 1667-1672
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The infection of human cells by HIV-1 virus can be mimicked by a fusion process between cells expressing the HIV envelope protein (Env) and cells expressing both human CD4 (huCD4) and appropriate human chemokine receptors. In this study, a macrophage-tropic (M-tropic) HIV cell-cell fusion assay was established that utilized huCD4, human CCR5 (huCCR5), and HIV ADAgp160 as fusion components and a Gal4/VP16-activated luciferase as a reporter system. By combining CHO cells expressing huCD4 and huCCR5 with CHO cells expressing HIV ADAgp160, a 300-fold increase in luciferase activity could be elicited relative to control. No luciferase activity was detected when HXB2gp160 (T-tropic) was used instead of ADAgp160 (M-tropic) as the fusion partner in the assay. Addition of anti-huCD4 (RPA-T4) or anti-huCCR5 (2D7) monoclonal antibodies in the assay inhibited the fusion event; in contrast, an anti-**CXCR4** (12G5) monoclonal antibody had little effect, indicating that the fusion assay was huCD4 and huCCR5 dependent. The cell-cell fusion occurred in a time-dependent manner; the maximum luciferase activity was detected about 8 h after mixing the cells. The fusion events could also be monitored by another reporter system in which Gal4/VP16 activated green fluorescent protein (GFP) was used as the reporter instead of luciferase. In combination with fluorescence microscopy, the GFP reporter system allowed visualization of the fusion events in real time. Compared with previously described **HIV fusion** models, this system has several advantages, including simplicity, sensitivity, and the ability to allow continuous monitoring of the HIV cell-cell fusion event. Finally, this cell-cell fusion system is easily adapted to study other **HIV fusion** events.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:765628 CAPLUS
DOCUMENT NUMBER: 130:138168
TITLE: The neutral glycosphingolipid globotriaosylceramide promotes fusion mediated by a CD4-dependent **CXCR4**-utilizing HIV type 1 envelope glycoprotein
AUTHOR(S): Puri, Anu; Hug, Peter; Jernigan, Kristine; Barchi, Joseph; Kim, Hee-Yong; Hamilton, Jillon; Wiels, Joelle; Murray, Gary J.; Brady, Roscoe O.; Blumenthal, Robert
CORPORATE SOURCE: Section of Membrane Structure and Function, Laboratory of Experimental and Computational Biology, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, Frederick, MD, 21702, USA
SOURCE: Proceedings of the National Academy of Sciences of the

United States of America (1998), 95(24), 14435-14440
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previously, the authors showed that the addition of human erythrocyte glycosphingolipids (GSLs) to nonhuman CD4+ or GSL-depleted human CD4+ cells rendered those cells susceptible to HIV-1 envelope glycoprotein-mediated cell fusion. Individual components in the GSL mixture were isolated by fractionation on a silica-gel column and incorporated into the membranes of CD4+ cells. GSL-supplemented target cells were then examined for their ability to fuse with TF228 cells expressing HIV-1LAI envelope glycoprotein. The authors found that one GSL fraction, fraction 3, exhibited the highest recovery of fusion after incorporation into CD4+ nonhuman and GSL-depleted HeLa-CD4 cells and that fraction 3 contained a single GSL fraction. Fraction 3 was characterized by MS, NMR spectroscopy, enzymic anal., and immunostaining with an anti-globotriaosylceramide (Gb3) antibody and was Gal(α1→4)Gal(β1→4)Glc-Cer (Gb3). The addition of fraction 3 or Gb3 to GSL-depleted HeLa-CD4 cells recovered fusion, but the addition of galactosylceramide, glucosylceramide, the monosialoganglioside, GM3, or α-galactosidase A-digested fraction 3 had no effect. Thus, the neutral GSL, Gb3, is required for CD4/**CXCR4**-dependent HIV-1 fusion.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:129239 CAPLUS
DOCUMENT NUMBER: 128:269372
TITLE: Recombinant human CXC-chemokine receptor-4 in melanophores are linked to Gi protein: seven transmembrane coreceptors for human immunodeficiency virus entry into cells
AUTHOR(S): Chen, Wen-Ji; Jayawickreme, Channa; Watson, Chris; Wolfe, Larry; Holmes, William; Ferris, Robert; Armour, Susan; Dallas, Walter; Chen, Grace; Boone, Larry; Luther, Michael; Kenakin, Terry
CORPORATE SOURCE: Department of Molecular Sciences, Glaxo Wellcome Research and Development, Research Triangle Park, NC, 27709, USA
SOURCE: Molecular Pharmacology (1998), 53(2), 177-181
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This article describes the transient expression of the CXC chemokine receptor-4 in Xenopus laevis melanophores and the resulting functional assay for the endogenous ligand for this receptor stromal cell-derived factor (SDF)-1α. Specifically, it will be shown that SDF-1α produces increased light transmittance in transfected cells that is consistent with the activation of Gi protein. This stimulus pathway is further implicated by the abolition of this response after pretreatment of the cells with pertussis toxin, a known method for the inactivation of Gi protein. The fact that SDF-1α does not produce responses in nontransfected cells and that treatment of the cells with 12G5, an antibody specific for the CXC chemokine receptor-4, eliminates this response indicates that this ligand produces responses by activation of this receptor in these cells. The possible relevance to human immunodeficiency virus (HIV) entry into cells was explored by observing the effects of SDF-1α on HIV-mediated cell fusion. It was found that SDF-1α blocked cell-to-cell fusion (as has been previously reported) at concns. 1200-fold greater than those required to produce Gi protein mediated responses. The implications of the functional assay to

screening for new drugs to block HIV-mediated fusion is discussed.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:395183 CAPLUS
DOCUMENT NUMBER: 127:120601
TITLE: Evolution of HIV-1 coreceptor usage through interactions with distinct CCR5 and **CXCR4** domains
AUTHOR(S): Lu, Zhao-hai; Berson, Joanne F.; Chen, Ying-hua; Turner, Julie D.; Zhang, Tian-yuan; Sharron, Matthew; Jenks, M. Harley; Wang, Zi-xuan; Kim, Jin; Rucker, Joseph; Hoxie, James A.; Peiper, Stephen C.; Doms, Robert W.
CORPORATE SOURCE: James Graham Brown Cancer Center, University Louisville, Louisville, KY, 40202, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(12), 6426-6431
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The chemokine receptor **CXCR4** functions as a fusion coreceptor for T cell tropic and dual-tropic HIV-1 strains. To identify regions of **CXCR4** that are important for coreceptor function, **CXCR4** -CXCR2 receptor chimeras were tested for the ability to support HIV-1 envelope (env) protein-mediated membrane fusion. Receptor chimeras containing the first and second extracellular loops of **CXCR4** supported fusion by T tropic and dual-tropic HIV-1 and HIV-2 strains and binding of a monoclonal antibody to **CXCR4**, 12G5, that blocks **CXCR4** -dependent infection by some virus strains. The second extracellular loop of **CXCR4** was sufficient to confer coreceptor function to CXCR2 for most virus strains tested but did not support binding of 12G5. Truncation of the **CXCR4** cytoplasmic tail or mutation of a conserved DRY motif in the second intracellular loop did not affect coreceptor function, indicating that phosphorylation of the cytoplasmic tail and the DRY motif are not required for coreceptor function. The results implicate the involvement of multiple **CXCR4** domains in HIV-1 coreceptor function, especially the second extracellular loop, though the structural requirements for coreceptor function were somewhat variable for different env proteins. Finally, a hybrid receptor in which the N terminus of **CXCR4** was replaced by that of CCR5 was active as a coreceptor for M tropic, T tropic, and dual-tropic env proteins. The authors propose that dual tropism may evolve in CCR5-restricted HIV-1 strains through acquisition of the ability to utilize the first and second extracellular loops of **CXCR4** while retaining the ability to interact with the CCR5 N-terminal domain.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:251532 CAPLUS
DOCUMENT NUMBER: 126:316221
TITLE: Differential regulation of HIV-1 fusion cofactor expression by CD28 costimulation of CD4+ T cells
AUTHOR(S): Carroll, Richard G.; Riley, James L.; Levine, Bruce L.; Feng, Yu; Kaushal, Sumesh; Ritchey, David W.; Bernstein, Wendy; Weislow, Owen S.; Brown, Charles R.; Berger, Edward A.; June, Carl H.; St. Louis, Daniel C.
CORPORATE SOURCE: Henry M. Jackson Foundation Advancement Military Med., Rockville, MD, 20850, USA
Science (Washington, D. C.) (1997), 276(5310), 273-276
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of CD4+ T lymphocytes from human immunodeficiency virus-type 1 (HIV-1)-infected donors with immobilized antibodies to CD3 and CD28 induces a virus-resistant state. This effect is specific for macrophage-tropic HIV-1. Transcripts encoding **CXCR4**/fusin, the fusion cofactor used by T cell line-tropic isolates, were abundant in CD3/CD28-stimulated cells, but transcripts encoding CCR5, the fusion cofactor used by macrophage-tropic viruses, were not detectable. Thus, CD3/CD28 costimulation induces an HIV-1-resistant phenotype similar to that seen in some highly exposed and HIV-uninfected individuals.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:250299 CAPLUS
DOCUMENT NUMBER: 126:316023
TITLE: **HIV fusion** cofactors. The chemokine receptor connection
AUTHOR(S): Uchida, Hiroyuki; Berger, Edward A.
CORPORATE SOURCE: Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: Jikken Igaku (1997), 15(2), 125-130
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 25 refs. Individual HIV-1 isolates vary markedly in their tropisms for infecting different CD4-pos. target cell types. Some isolates (macrophage-tropic) infect macrophages but not continuous T-lymphocyte cell lines, while others (T-cell line-tropic) display the opposite preference. We have shown that the cytotropism of different HIV variants are due to the inherent fusion specificities of the corresponding Env proteins, which in turn result from the ability of each Env to use distinct "fusion cofactors" that are differentially expressed on various CD4-pos. cell types. Using a novel functional cDNA screening method, we identified a fusion cofactor for T-cell line-tropic isolates, and designated this mol. fusin (**CXCR4**). Subsequently we identified another cofactor, CCR5 (CC CKR5), that functions preferentially for macrophage-tropic variants. Both cofactors are members of the chemokine receptor family of G protein-coupled receptors. Primary HIV-1 isolates from diverse genetic subtypes function with CCR5 and/or fusin (and in some cases with other chemokine receptors). We determined that signaling through G proteins is not required for fusion cofactor activity. Studies are in progress to identify functional determinants in the Env/cofactor interactions. We observed that fusin and CCR5 expression is regulated differently upon T-cell activation, suggesting implications for HIV replication in vivo. Of particular interest are findings indicating that genetic alterations in the fusion cofactors can directly influence susceptibility to HIV infection, and possibly rates of AIDS progression in infected persons. The identification of the fusion cofactors suggests a means to develop small animal models susceptible to HIV infection. Moreover, the cofactors represent new mol. targets for the design of anti-AIDS therapeutic agents that block the fusion reactions involved in HIV entry and tropism.

L5 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:57315 CAPLUS
DOCUMENT NUMBER: 126:88231
TITLE: Inhibition of human immunodeficiency virus fusion by a monoclonal antibody to a coreceptor (**CXCR4**) is both cell type and virus strain dependent
AUTHOR(S): McKnight, Aine; Wilkinson, David; Simmons, Graham;

Talbot, Simon; Picard, Laurent; Ahuja, Mena; Marsh, Mark; Hoxie, James A.; Clapham, Paul R.

CORPORATE SOURCE: Chester Beatty Laboratories, Institute of Cancer Research, London, SW3 6JB, UK

SOURCE: Journal of Virology (1997), 71(2), 1692-1696
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **CXCR4** (also termed fusion, LESTR, or HUMSTR) is a member of the G-protein-coupled chemokine receptor family with seven membrane-spanning domains. **CXCR4** acts as a coreceptor for syncytium-inducing human immunodeficiency virus type 1 (HIV-1) strains, conferring entry into CD4+ cells. We show here that a novel mouse monoclonal antibody (12G5) that recognizes **CXCR4** blocked cell-to-cell fusion and cell free-virus infection of **CXCR4**+ CD4+ RD rhabdomyosarcoma cells by seven HIV-1 and HIV-2 strains that had various cell tropisms for different CD4+ human cell types. Yet the majority of the members of the same virus panel resisted 12G5 inhibition on T-cell lines. When inhibition was observed on these cell types, it was both cell type and virus strain dependent. In at least one situation, 12G5 failed to block LAI infection of cells expressing **CXCR4** as the only available coreceptor. Our observations suggest that **CXCR4** could be processed or presented differently depending on the cell type, allowing some strains to evade 12G5 inhibition. Alternatively, since several of the viruses could infect certain **CXCR4**- CD4+ cell lines, it is conceivable that alternative coreceptors are active, enabling individual HIV strains to choose between compatible coreceptors during entry into cells. Moreover, the strain dependency of 12G5 inhibition implies that the interaction of different HIVs with **CXCR4** varies.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:148781 BIOSIS

DOCUMENT NUMBER: PREV200400152569

TITLE: Compensatory link between fusion and endocytosis of human immunodeficiency virus type 1 in human CD4 T lymphocytes.

AUTHOR(S): Schaeffer, Evelyne; Soros, Vanessa B.; Greene, Warner C. [Reprint Author]

CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, P.O. Box 419100, San Francisco, CA, 94141-9100, USA
wgreene@gladstone.ucsf.edu

SOURCE: Journal of Virology, (February 2004) Vol. 78, No. 3, pp. 1375-1383. print.
ISSN: 0022-538X (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB Virions of the type 1 human immunodeficiency virus (HIV-1) can enter target cells by fusion or endocytosis, with sharply different functional consequences. Fusion promotes productive infection of the target cell, while endocytosis generally leads to virion inactivation in acidified endosomes or degradation in lysosomes. Virion fusion and endocytosis occur equally in T cells, but these pathways have been regarded as independent because endocytosis of HIV virions requires neither CD4 nor CCR5/**CXCR4** engagement in HeLa-CD4 cells. Using flow cytometric techniques to assess the binding and entry of green fluorescent protein (GFP)-Vpr-labeled HIV virions into primary peripheral blood mononuclear cells, we have found that **HIV fusion** and endocytosis are restricted to the CD4-expressing subset of cells and that both pathways commonly require the initial binding of HIV virions to surface

CD4 receptors. Blockade of **CXCR4**-tropic HIV virion fusion with AMD3100, a **CXCR4**-specific entry inhibitor, increased virion entry via the endocytic pathway. Similarly, inhibition of endosome acidification with bafilomycin A1, concanamycin A, or NH4Cl enhanced entry via the fusion pathway. Although fusion remained dependent on CD4 and chemokine receptor binding, the endosome inhibitors did not alter surface expression of CD4 and **CXCR4**. These results suggest that fusion in the presence of the endosome inhibitors likely occurs within nonacidified endosomes. However, the ability of these inhibitors to impair vesicle trafficking from early to late endosomes in some cells could also increase the recycling of these virion-containing endosomes to the cell surface, where fusion occurs. In summary, our results reveal an unexpected, CD4-mediated reciprocal relationship between the pathways governing HIV virion fusion and endocytosis.

L5 ANSWER 18 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:76039 BIOSIS
DOCUMENT NUMBER: PREV200400077333
TITLE: Establishment of an HIV cell-cell fusion assay by using two genetically modified HeLa cell lines and reporter gene.
AUTHOR(S): Sakamoto, Tatsunori; Ushijima, Hiroshi [Reprint Author]; Okitsu, Shoko; Suzuki, Eiko; Sakai, Koji; Morikawa, Shigeru; Muller, Werner E. G.
CORPORATE SOURCE: Department of Developmental Medical Sciences, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan
ushijima@m.u-tokyo.ac.jp
SOURCE: Journal of Virological Methods, (December 2003) Vol. 114, No. 2, pp. 159-166. print.
CODEN: JVMEDH. ISSN: 0166-0934.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004

AB Infection of human cells with the human immunodeficiency virus type I (HIV-1) can be mimicked by a fusion process between cells expressing the HIV envelope protein (Env) and cells expressing both human CD4 together with the appropriate human chemokine receptors. In this study, a T-tropic HIV cell-cell fusion assay was established that utilized CD4, human **CXCR4** and HIV NL4-3 gp160 as fusion components and a T7 polymerase-activated luciferase as a reporter system. The HeLa T4 cells used, expressed CD4 and **CXCR4**, and the applied HeLa KS386 cells expressed HIV NL4-3 gp160. By combining HeLaT4 cells with HeLa KS386 cells, an approximately about 100- to 300-fold increase in luciferase activity could be elicited relative to the control. The addition of anti-CD4 monoclonal antibody (Mab) (RPA-T4) or anti-**CXCR4** Mab (12G5) in the assay significantly inhibited the fusion event; in contrast, an anti-CCR5 Mab (2D7) had no effect, indicating that the fusion assay was CD4 and **CXCR4** dependent. In this report, fusion events could be monitored by both the luciferase reporter system and syncytia formation. Fusion events were monitored and compared using these two approaches. The luciferase reporter system was found to be more sensitive than syncytia formation. Moreover, compared with previous **HIV fusion** models, such as using recombinant vaccinia viruses, this system has several advantages, including simplicity and sensitivity. Finally, the system provides a powerful tool to study fusion mechanisms mediated by T-tropic HIV gp160, as well as to screen for fusion-blocking antibodies and antiviral agents.

L5 ANSWER 19 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:528897 BIOSIS
DOCUMENT NUMBER: PREV200100528897

TITLE: Antigenic properties of the human immunodeficiency virus envelope during cell-cell fusion.
AUTHOR(S): Finnegan, Catherine M.; Berg, Werner; Lewis, George K.; DeVico, Anthony L. [Reprint author]
CORPORATE SOURCE: Institute of Human Virology, 725 W. Lombard St., N649, Baltimore, MD, 21201, USA
devico@umbi.umd.edu
SOURCE: Journal of Virology, (November, 2001) Vol. 75, No. 22, pp. 11096-11105. print.
CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Nov 2001
Last Updated on STN: 23 Feb 2002

AB Human immunodeficiency virus (**HIV**) **fusion** and entry involves sequential interactions between the viral envelope protein, gp120, cell surface CD4, and a G-protein-coupled coreceptor. Each interaction creates an intermediate gp120 structure predicted to display distinct antigenic features, including key functional domains for viral entry. In this study, we examined the disposition of these features during the fusion of HeLa cells expressing either HIVHXB2 envelope (Env cells) or **CXCR4** and CD4 (target cells). Cell-cell fusion, indicated by cytoplasmic dye transfer, was allowed to progress for various times and then arrested. The cells were then examined for reactivity with antibodies directed against receptor-induced epitopes on gp120. Analyses of cells arrested by cooling to 4degreeC revealed that antibodies against the CD4-induced coreceptor-binding domain, i.e., 17b, 48d, and CG10, faintly react with Env cells even in the absence of target cell or soluble CD4 (sCD4) interactions. Such reactivity increased after exposure to sCD4 but remained unchanged during fusion with target cells and was not intensified at the Env-target cell interface. Notably, the antibodies did not react with Env cells when treated with a covalent cross-linker either alone or during fusion with target cells. Immunoreactivity could not be promoted or otherwise altered on either temperature arrested or cross-linked cells by preventing coreceptor interactions or by using a 17b Fab. In comparison, two other gp120-CD4 complex-dependent antibodies against epitopes outside the coreceptor domain, 8F101 and A32, exhibited a different pattern of reactivity. These antibodies reacted with the Env-target cell interface only after 30 min of cocultivation, concurrent with the first visible transfer of cytoplasmic dye from Env to target cells. At later times, the staining surrounded entire syncytia. Such binding was entirely dependent on the formation of gp120-CD4-**CXCR4** tricomplexes since staining was absent with SDF-treated or coreceptor-negative target cells. Overall, these studies show that access to the CD4-induced coreceptor-binding domain on gp120 is largely blocked at the fusing cell interface and is unlikely to represent a target for neutralizing antibodies. However, new epitopes are presented on intermediate gp120 structures formed as a result of coreceptor interactions. Such findings have important implications for HIV vaccine approaches based on conformational alterations in envelope structures.

L5 ANSWER 20 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:77292 BIOSIS
DOCUMENT NUMBER: PREV200000077292
TITLE: New reporter cell lines to study macrophage-tropic HIV envelope protein-mediated cell-cell fusion.
AUTHOR(S): Hong, Yu-Long; Wu, Lan-Hsin; Cui, Mei; McMaster, Gary; Hunt, Stephen W., III; Chung, Fu-Zon [Reprint author]
CORPORATE SOURCE: Department of Molecular Biology, Parke-Davis Pharmaceutical Research, 2800 Plymouth Rd., Ann Arbor, MI, USA
SOURCE: AIDS Research and Human Retroviruses, (Dec., 1999) Vol. 15, No. 18, pp. 1667-1672. print.
CODEN: ARHRE7. ISSN: 0889-2229.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Feb 2000
Last Updated on STN: 3 Jan 2002

AB The infection of human cells by HIV-1 virus can be mimicked by a fusion process between cells expressing the HIV envelope protein (Env) and cells expressing both human CD4 (huCD4) and appropriate human chemokine receptors. In this study, a macrophage-tropic (M-tropic) HIV cell-cell fusion assay was established that utilized huCD4, human CCR5 (huCCR5), and HIV ADAgp160 as fusion components and a Gal4/VP16-activated luciferase as a reporter system. By combining CHO cells expressing huCD4 and huCCR5 with CHO cells expressing HIV ADAgp160, a 300-fold increase in luciferase activity could be elicited relative to control. No luciferase activity was detected when HXB2gp160 (T-tropic) was used instead of ADAgp160 (M-tropic) as the fusion partner in the assay. Addition of anti-huCD4 (RPA-T4) or anti-huCCR5 (2D7) monoclonal antibodies in the assay significantly inhibited the fusion event; in contrast, an anti-**CXCR4** (12G5) monoclonal antibody had little effect, indicating that the fusion assay was huCD4 and huCCR5 dependent. The cell-cell fusion occurred in a time-dependent manner; the maximum luciferase activity was detected about 8 hr after mixing the cells. The fusion events could also be monitored by another reporter system in which Gal4/VP16 activated green fluorescent protein (GFP) was used as the reporter instead of luciferase. In combination with fluorescence microscopy, the GFP reporter system allowed visualization of the fusion events in real time. Compared with previously described **HIV fusion** models, this system has several advantages, including simplicity, sensitivity, and the ability to allow continuous monitoring of the HIV cell-cell fusion event. Finally, this cell-cell fusion system is easily adapted to study other **HIV fusion** events.

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=> "HIV entry inhibitor"
L11          69 "HIV ENTRY INHIBITOR"

=> "fusion" (1) L11
L12          17 "FUSION" (L) L11

=> CXCR4 and L12
L13           4 CXCR4 AND L12

=> D L13 IBIB ABS 1-4
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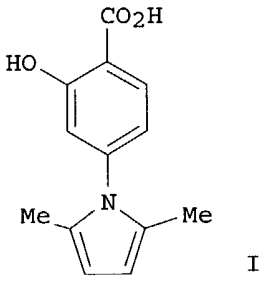
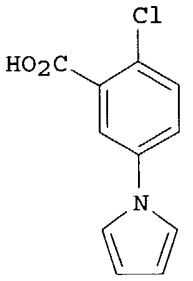
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047730	A2	20040610	WO 2003-US36359	20031112
WO 2004047730	A3	20040916		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004116427	A1	20040617	US 2003-706027	20031113
PRIORITY APPLN. INFO.:			US 2002-428055P P	20021121
OTHER SOURCE(S):	MARPAT 141:17579			

GI



I



II

AB A group of compds. that inhibit HIV replication by blocking HIV entry was identified. Two representative compds., designated NB-2 (I) and NB-64 (II), inhibited HIV replication (p24 production) with IC50 values < 0.5 μg/mL. It was proved that NB-2 and NB-64 are **HIV entry inhibitors** by targeting the HIV gp41 since: (1) they inhibited HIV-mediated cell **fusion**; (2) they inhibited HIV replication only when they were added to the cells less than one hour after virus addition; (3) they did not block the gp120-CD4 binding; (4) they did not interact with the co-receptor **CXCR4** since they failed to block anti-**CXCR4** antibody binding to **CXCR4**-expressing cells; (5) they blocked the formation of the gp41 core that is detected by sandwich enzyme linked immunosorbent assay (ELISA) using a conformation-specific Mab NC-1; (6) they inhibited the formation of the gp41 six-helix bundle revealed by fluorescence native-polyacrylamide gel electrophoresis (FN-PAGE); and (7) they blocked binding of D-peptide to the hydrophobic cavity within gp41 coiled coil domain, modeled by peptide IQN17. These results suggested that NB-2 and NB-64 may interact with the hydrophobic cavity and block the formation of the **fusion**-active gp41 coiled coil domain, resulting in inhibition of HIV-1 mediated membrane **fusion** and virus entry.

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:718520 CAPLUS
DOCUMENT NUMBER:	140:86912
TITLE:	Inhibitors of the entry of HIV into host cells
AUTHOR(S):	Meanwell, Nicholas A.; Kadow, John F.
CORPORATE SOURCE:	Department of Chemistry, Bristol-Myers Squibb

Pharmaceutical Research Institute, Wallingford, CT, 06492, USA
SOURCE: Current Opinion in Drug Discovery & Development (2003), 6(4), 451-461
CODEN: CODDFF; ISSN: 1367-6733
PUBLISHER: Current Drugs
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The development of mechanistic insight into the process by which HIV enters host cells has revealed a panoply of targets that offer considerable potential as sites for pharmacol. intervention. The gp120/gp41 protein complex, expressed on the virion surface, mediates HIV entry by a process initiated by the engagement of the host cell receptor CD4. Subtle conformational changes triggered by this interaction expose elements of gp120 to the seven-transmembrane, G protein-coupled chemokine receptors CCR5 or **CXCR4** expressed on host cells, a contact that relieves constraints imposed on gp41 by gp120. This leads to a major conformational rearrangement of gp41, which results in the insertion of the **fusion** peptide into the host cell membrane and the assembly of the amino terminus heptad repeat into a trimeric form that is subsequently recognized by the carboxy terminal heptad repeat. The latter process leads to juxtaposition of the viral and host cell membranes, a prelude to **fusion**. The most prominent strategies and targets that are actively being exploited as drug discovery opportunities are inhibition of the attachment of HIV to host cells, blockade of chemokine receptors and interference with the function of gp41. Inhibitors of each of these steps in the HIV entry process with potential clin. relevance are reviewed in the context of their status in the drug development process. The most significant entity to emerge from this area of research to date is enfuvirtide, a 36-amino acid derivative that interferes with the function of gp41. Enfuvirtide is the first **HIV entry inhibitor** to be granted a license for marketing (it was approved in the US and Europe in Mar. 2003), and its introduction portends the beginning of what promises to be an exciting new era of HIV therapy.
REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:661381 CAPLUS
DOCUMENT NUMBER: 140:104193
TITLE: Virus entry as a target for anti-HIV intervention
AUTHOR(S): Este, Jose A.
CORPORATE SOURCE: Retrovirology Laboratory irsiCaixa, Hospital Universitari Germans Trias i Pujol, Universitat Autonoma de Barcelona, Badalona, 08916, Spain
SOURCE: Current Medicinal Chemistry (2003), 10(17), 1617-1632
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The replicative cycle of the human immunodeficiency virus (HIV) can be interrupted at several stages. Until recently only the viral reverse transcriptase and protease were the only enzymes targeted by antiretroviral agents. However, the first **HIV entry inhibitor** (T-20, Enfuvirtide, Fuseon) to be used in humans has been approved by the Food and Drug Administration (FDA). The HIV entry process is considered as an attractive target for chemotherapeutic intervention, as blocking HIV entry into its target cell leads to suppression of viral infectivity, replication and the cytotoxicity induced by virus-cell contacts. HIV-1 entry into target cells is a multistep process: virus attachment is initiated by the binding of trimeric envelope glycoprotein gp120 complexes on the virions to glycosylated T-cell surface receptor (CD4) and IIIV GPCR coreceptors (CCR5 or **CXCR4**) leading to envelope glycoprotein gp41-dependent **fusion**-pore formation

and membrane **fusion**. A number of compds. are being developed to specifically target each of these steps leading to virus entry and some compds. have reached early clin. development. Conversely, agents such as the CCR5 antagonist Tak-779 and the **CXCR4** antagonist AMD3100 are not longer being thought as relevant anti-HIV agents but have given way to new analogs with improved properties. This review summarizes the current state of **HIV entry inhibitors**, their mechanisms of action and their therapeutic value against HIV infection and AIDS.

REFERENCE COUNT: 151 THERE ARE 151 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:71735 BIOSIS
DOCUMENT NUMBER: PREV200300071735
TITLE: Sensitivity of HIV-1 to entry inhibitors correlates with envelope/coreceptor affinity, receptor density, and fusion kinetics.
AUTHOR(S): Reeves, Jacqueline D. [Reprint Author]; Gallo, Stephen A.; Ahmad, Navid; Miamidian, John L.; Harvey, Phoebe E.; Sharron, Matthew; Pohlmann, Stefan; Sfakianos, Jeffrey N.; Derdeyn, Cynthia A.; Blumenthal, Robert; Hunter, Eric; Doms, Robert W. [Reprint Author]
CORPORATE SOURCE: Department of Microbiology, University of Pennsylvania, 3610 Hamilton Walk, 225 Johnson Pavilion, Philadelphia, PA, 19104, USA
jreeves@mail.med.upenn.edu; doms@mail.med.upenn.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (December 10 2002) Vol. 99, No. 25, pp. 16249-16254. print.
ISSN: 0027-8424 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB **HIV entry inhibitors** include coreceptor antagonists and the **fusion** inhibitor T-20. T-20 binds the first helical region (HR1) in the gp41 subunit of the viral envelope (Env) protein and prevents conformational changes required for membrane **fusion**. HR1 appears to become accessible to T-20 after Env binds CD4, whereas coreceptor binding is thought to induce the final conformational changes that lead to membrane **fusion**. Thus, T-20 binds to a structural intermediate of the **fusion** process. Primary viruses exhibit considerable variability in T-20 sensitivity, and determinants outside of HR1 can affect sensitivity by unknown mechanisms. We studied chimeric Env proteins containing different V3 loop sequences and found that gp120/coreceptor affinity correlated with T-20 and coreceptor antagonist sensitivity, with greater affinity resulting in increased resistance to both classes of entry inhibitors. Enhanced affinity resulted in more rapid **fusion** kinetics, reducing the time during which Env is sensitive to T-20. Reduced coreceptor expression levels also delayed **fusion** kinetics and enhanced virus sensitivity to T-20, whereas increased coreceptor levels had the opposite effect. A single amino acid change (K421D) in the bridging sheet region of the primary virus strain YU2 reduced affinity for CCR5 and increased T-20 sensitivity by about 30-fold. Thus, mutations in Env that affect receptor engagement and membrane **fusion** rates can alter entry inhibitor sensitivity. Because coreceptor expression levels are typically limiting in vivo, individuals who express lower coreceptor levels may respond more favorably to entry inhibitors such as T-20, whose effectiveness we show depends in part on **fusion** kinetics.